New Trends in the Surgical Management of Cervical Carcinoma

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Global Female Cancer : Incidence & Mortality (2002)

	Incidence			Mortality		
		Crude rate	ASR		Crude Mortality Rate	ASR
Breast	**1151298**	37.4	37.4	**410712**	13.3	13.2
Cervix	**493243**	16	16.2	**273505**	8.9	9
Colorectal	**472687**	15.4	14.6	**250532**	8.1	7.6
Lung	**386891**	12.6	12.1	**330786**	10.7	10.3
Stomach	**330518**	10.7	10.4	**254297**	8.3	7.9
Ovary	**204499**	6.6	6.6	**124860**	4.1	4
Corpus uteri	**198783**	6.5	6.5	**50327**	1.6	1.6

Cervical Cancer: Incidence & Mortality (2002)

	Incidence			**Mortality**		
		Crude rate	ASR		Crude Mortality Rate	ASR
World	**493243**	16	16.2	**273505**	8.9	9
Developed	**83437**	13.6	10.3	**39512**	6.4	4
Developing	**409404**	16.5	19.1	**233776**	9.5	11.2
Egypt	**2713**	7.8	9.7	**2178**	6.3	7.9

Early Cancer Detection Unit
Ain Shams University
1992-2006

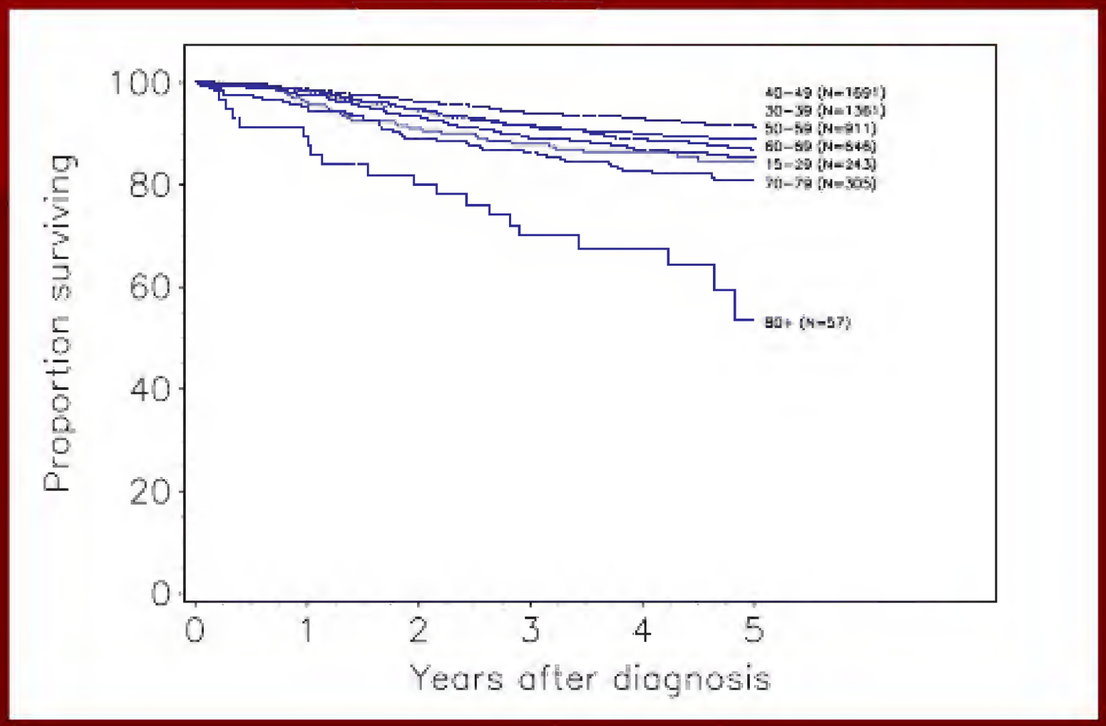
Endometrial cancer	**521** + 34 metastatic
Cervical cancer	**517** + 111 metastatic
Ovarian cancer	**323** epithelial **68** non epithelial
Vulval cancer	**98**

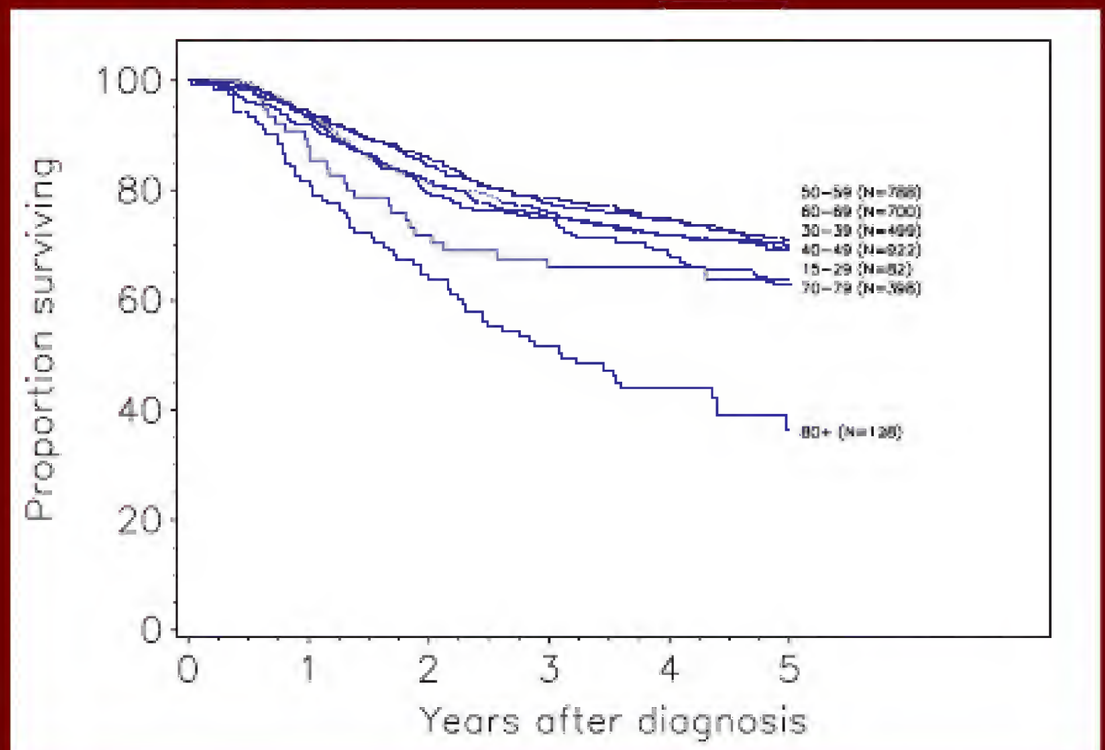
Overall Survival (*FIGO reports 2006)*

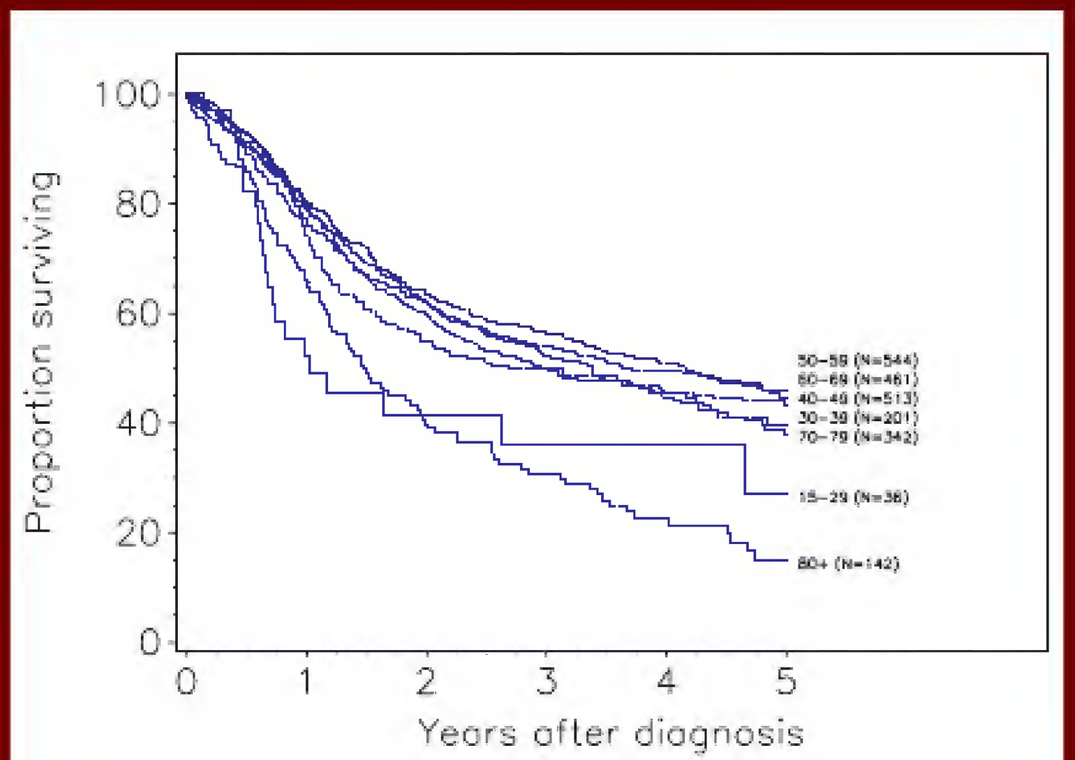
Year	Patients	Survival (%)
1973–75	34178	55.7
1976–78	32428	55.0
1979–81	31543	53.5
1982–86	32052	59.8
1987–89	22428	65.0
1990–92	12153	65.4
1993–95	11709	72.2
1996–98	10525	69.9
1999–2001	15081	69.6
	202097	

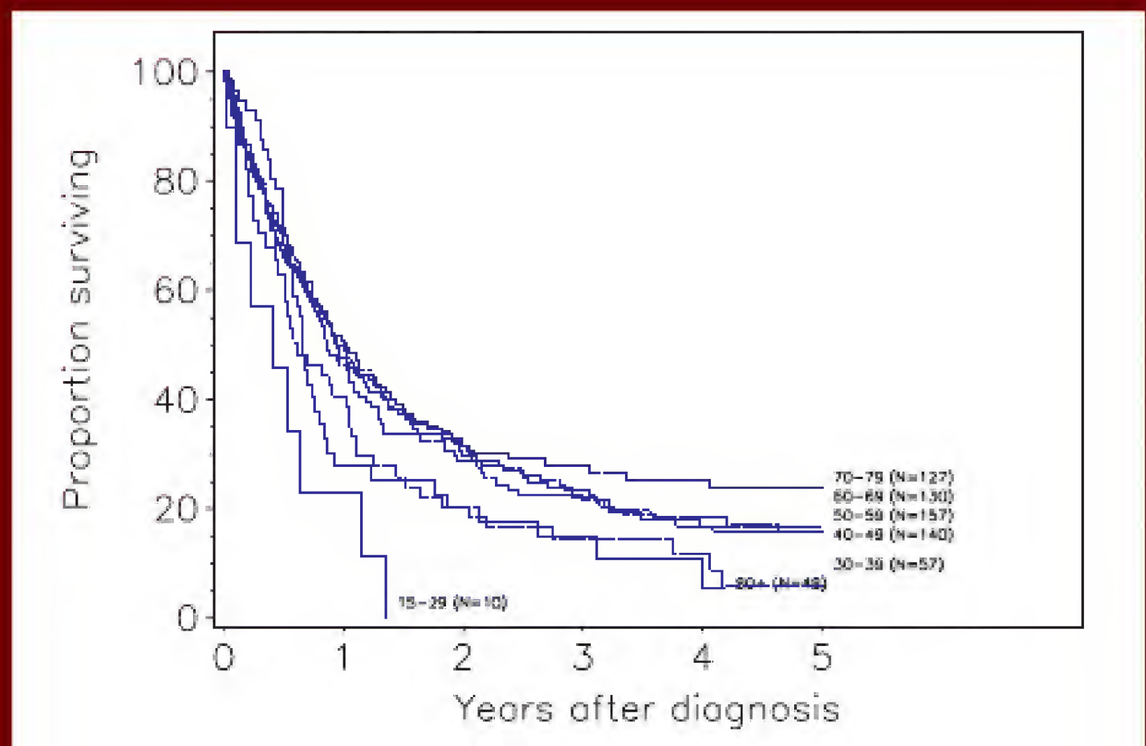
Survival by age in various stages

FIGO report 2006



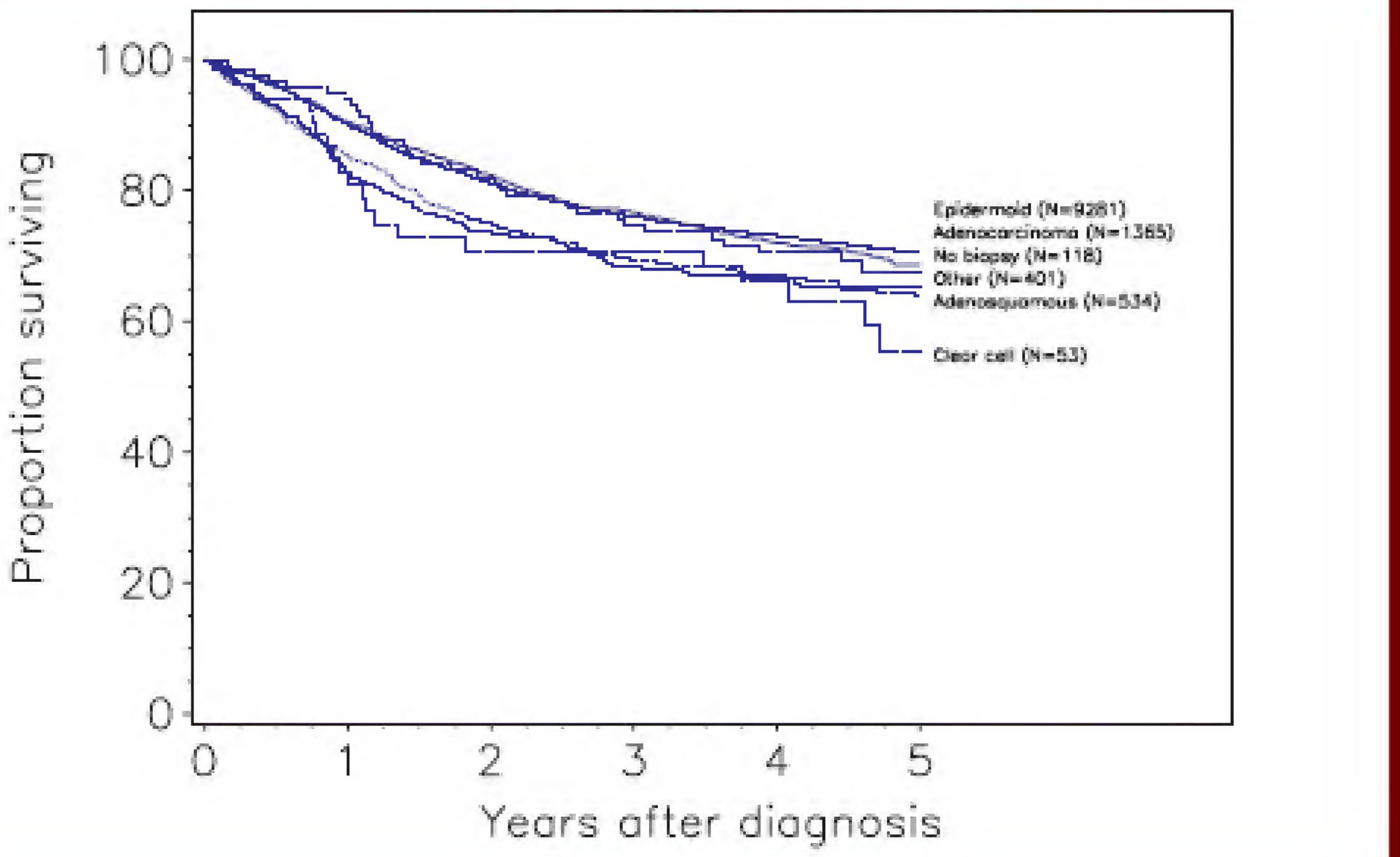






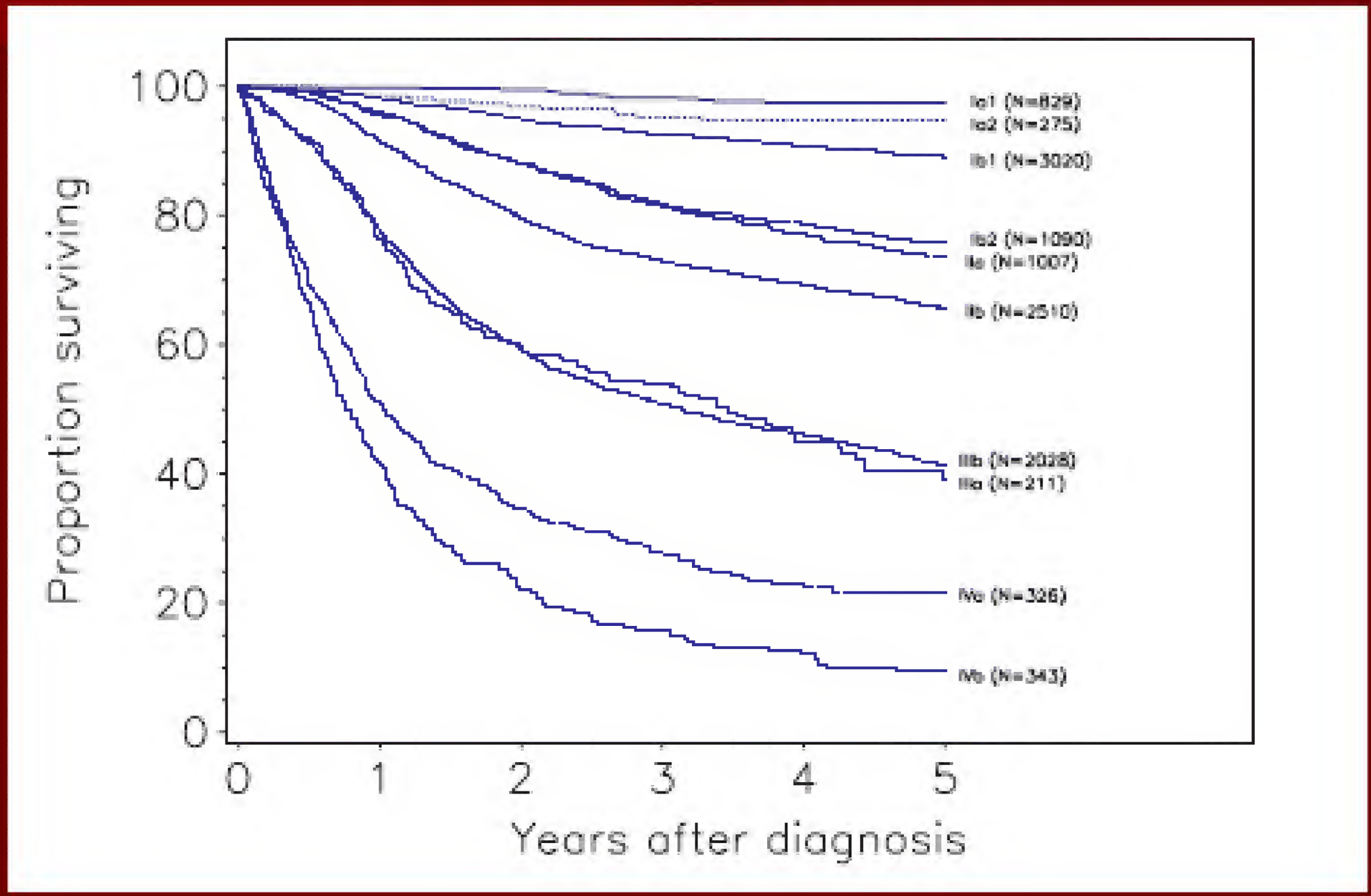
Survival by histologic type

FIGO report 2006



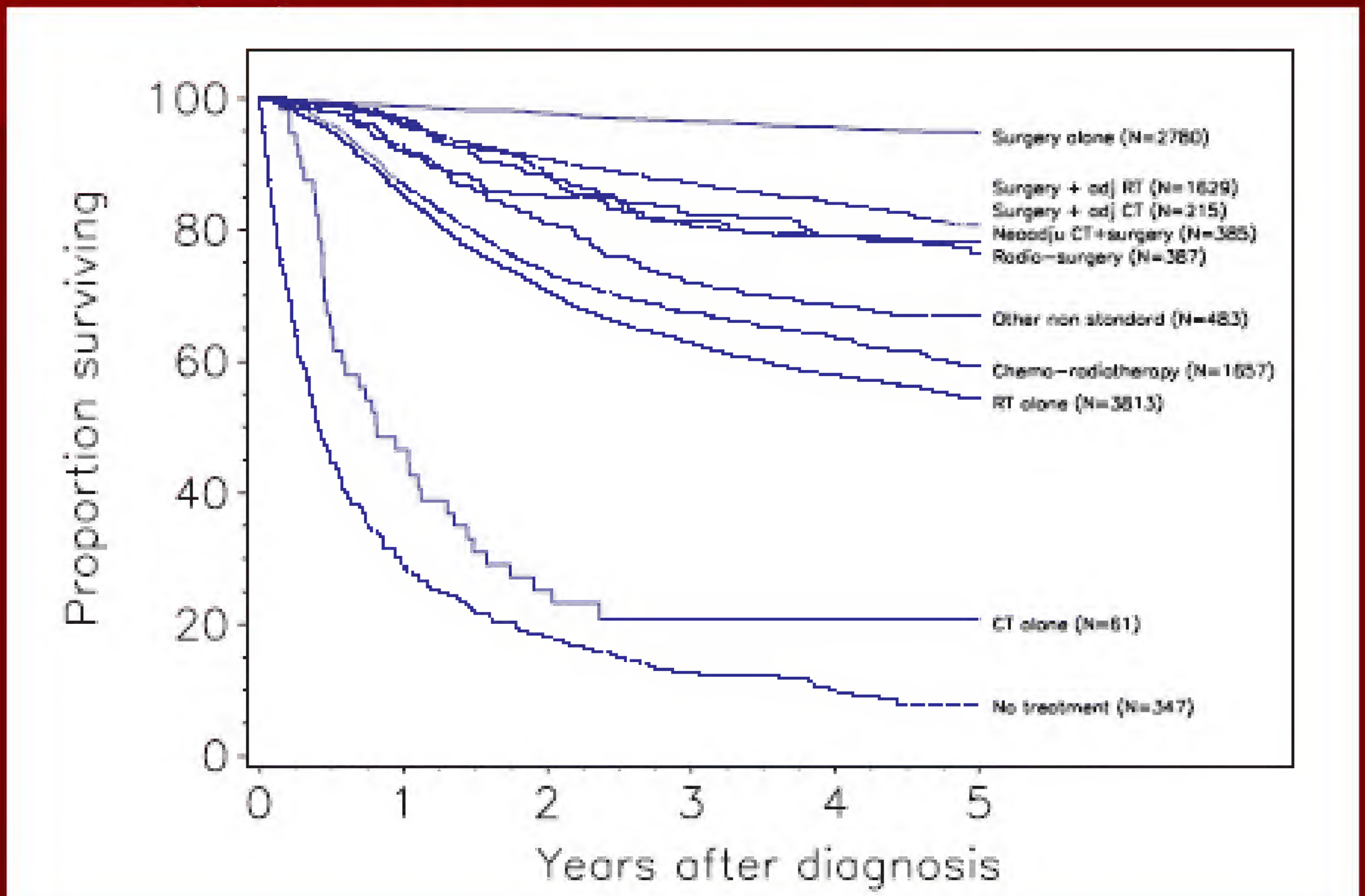
Survival by FIGO stage

FIGO report 2006



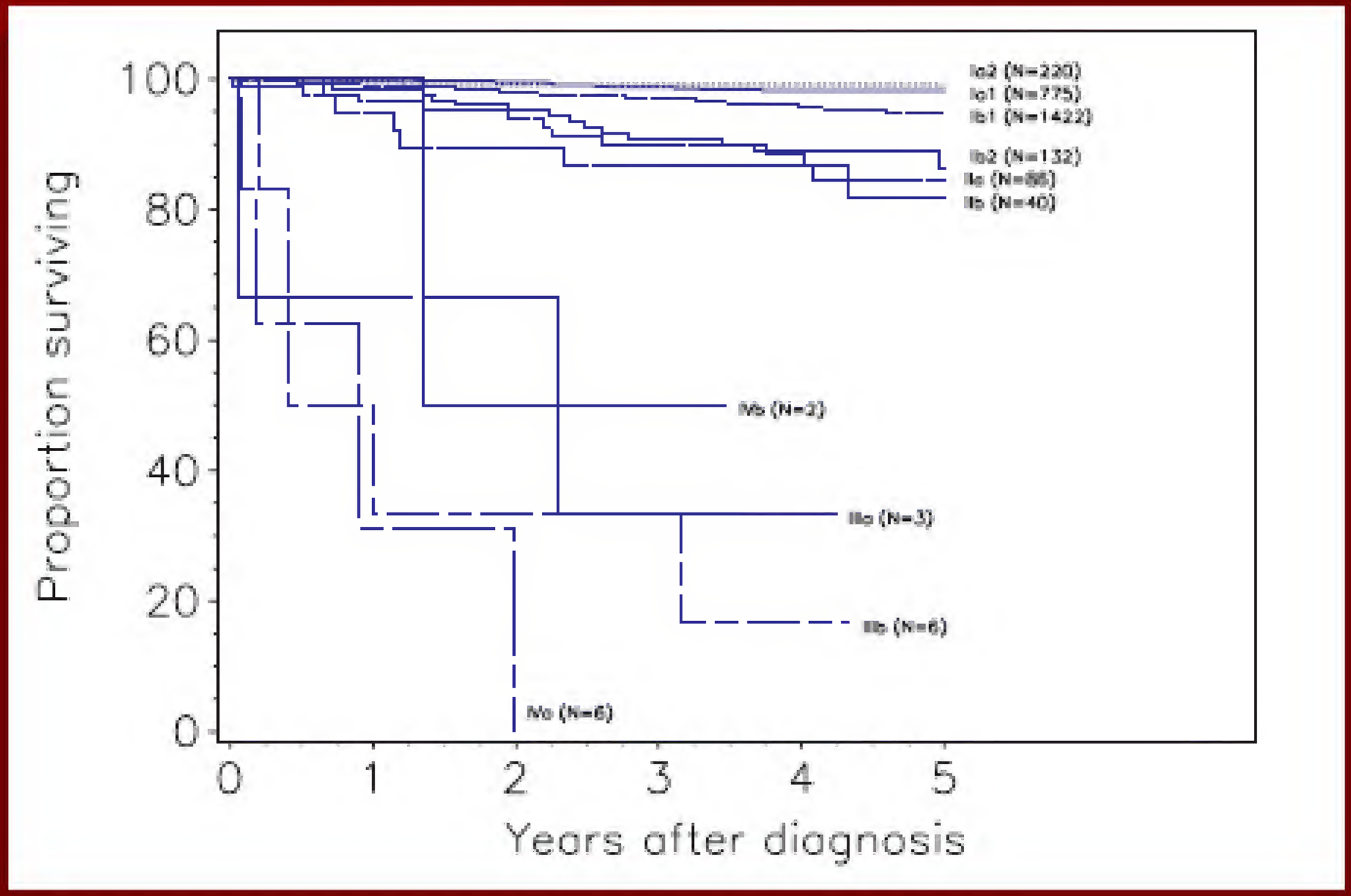
Survival by mode of treatment

FIGO report 2006



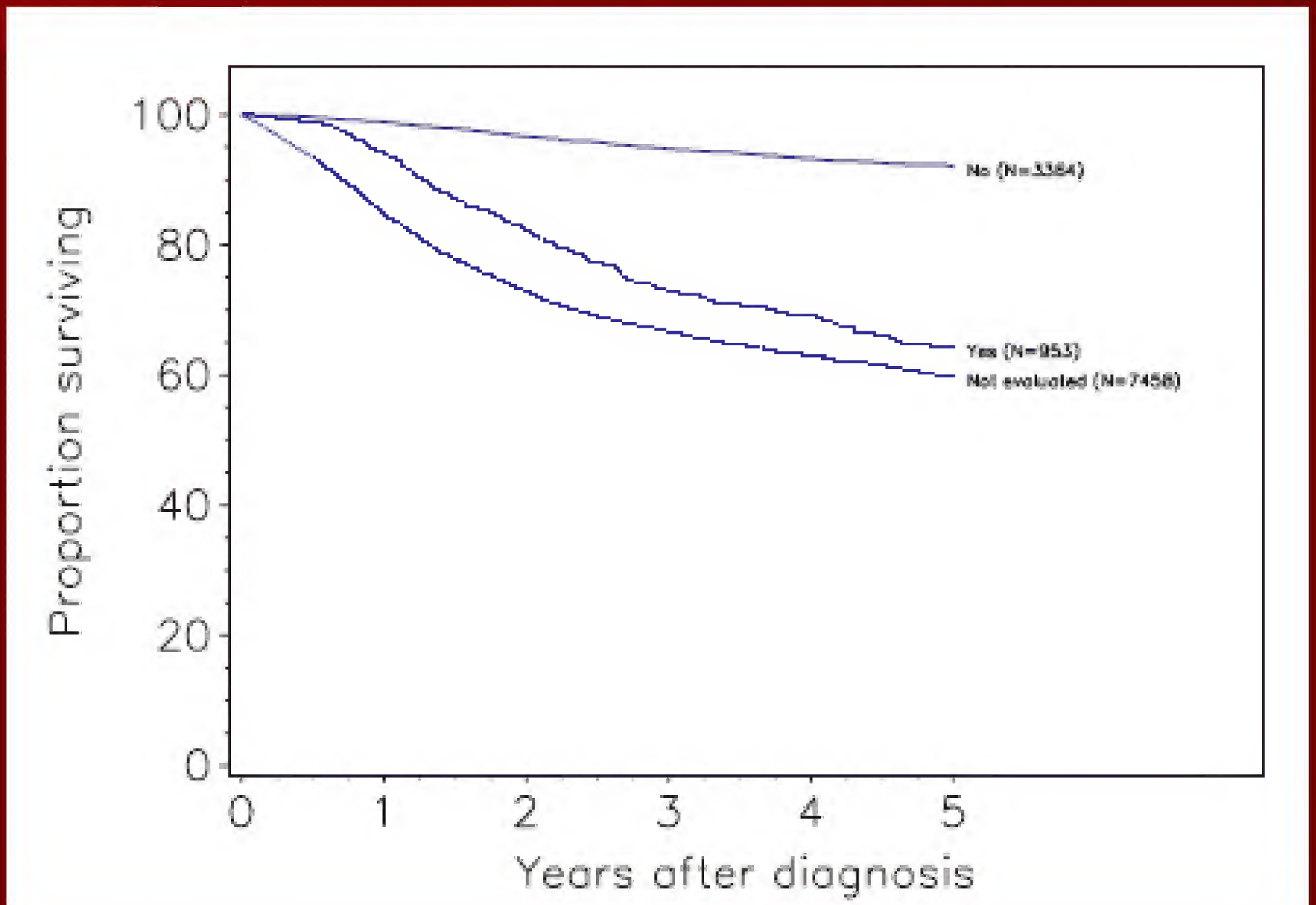
Survival by surgery only

FIGO report 2006



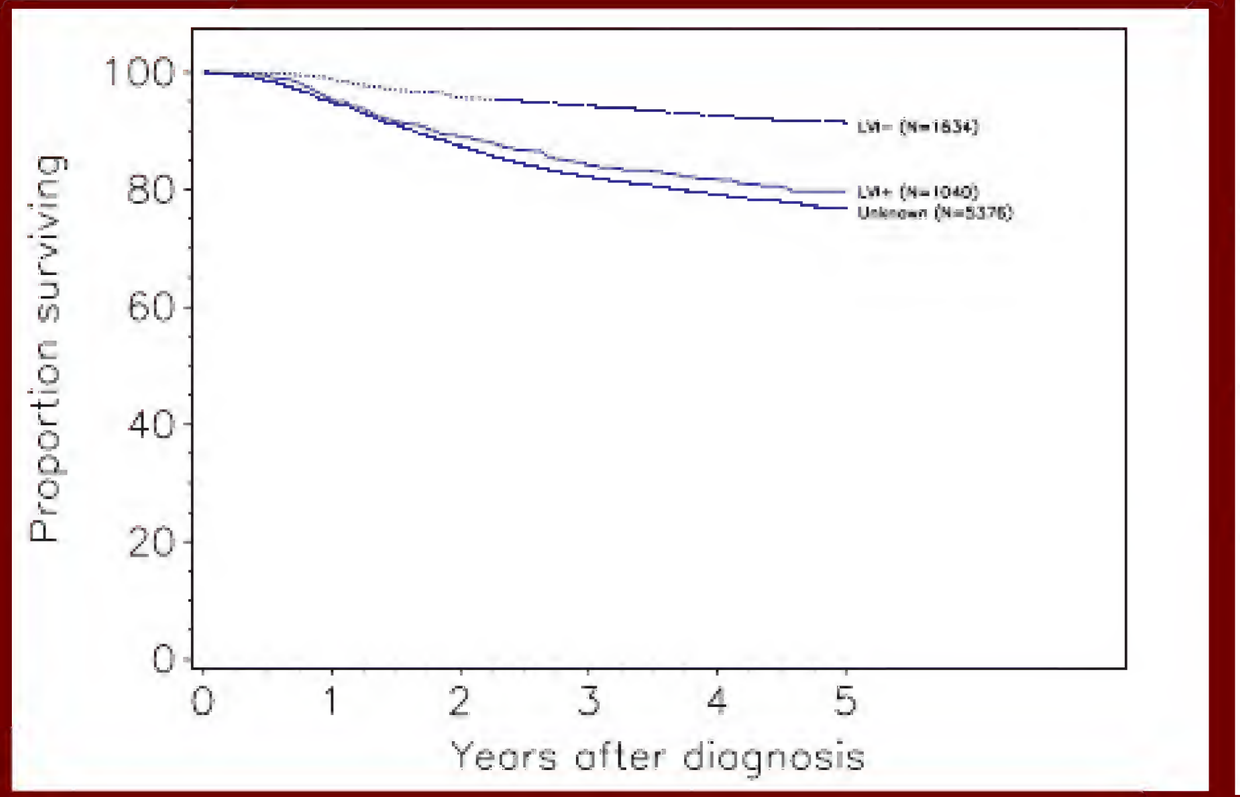
Survival by lymph node status

FIGO report 2006

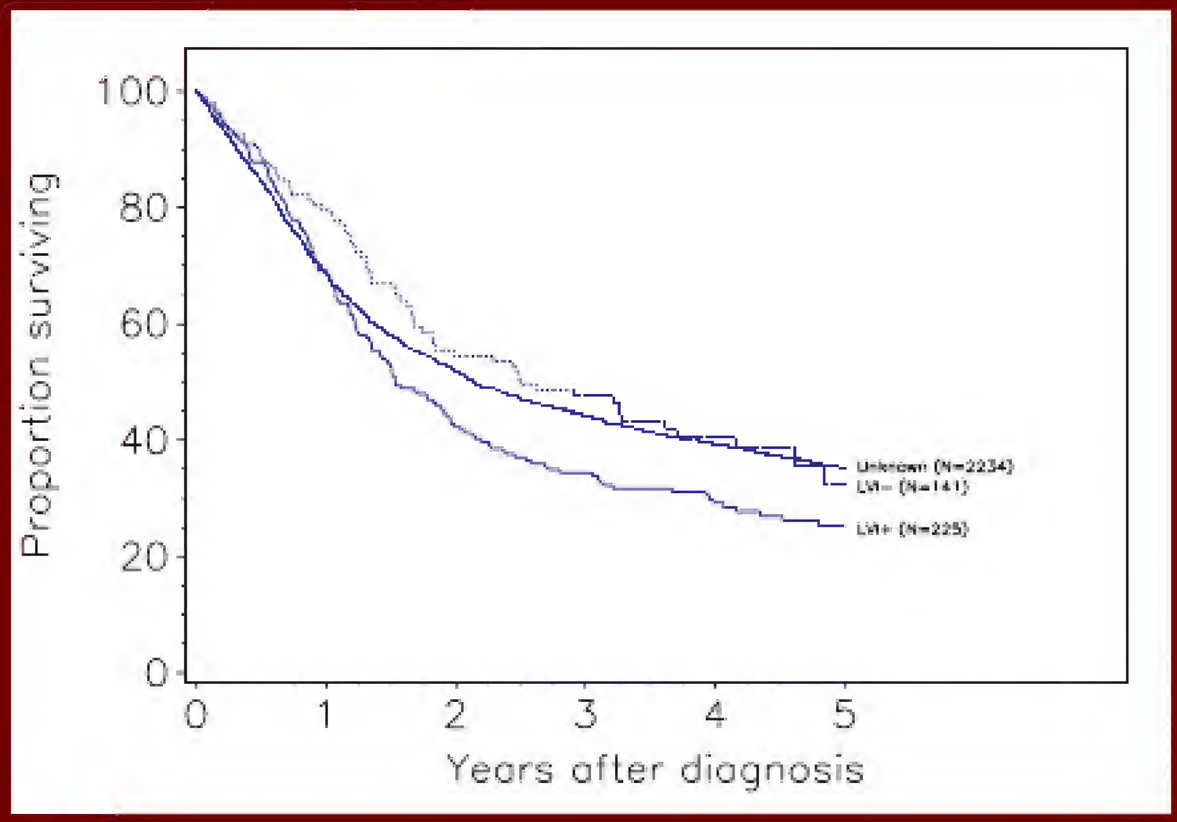


Survival by lymph-vascular involvement (LVI)

Stage I/II



Stage III/IV



- A tendency for increased incidence in younger age groups has been reported *(Wu et al. 2005)*

- Treatment of cervical cancer has been essentially dependent on stage

- Successful screening programs in many western countries have resulted in significant decrease in mortality rates and improved detection at earlier stages *(Peto et al. 2004)*

Directions and Developments

- Minimal access surgery

- More refined surgical radicality to preserve function or fertility and improve quality of life without deteriorating cure or patients' survival rates.

- A trend for surgically staging the disease for better definition of treatment options with the spreading and improved use of laparoscopy

- Down staging with neo-adjuvant chemo-therapy

Surgical options

- Fertility preserving options:
  - Conization
  - Radical trachelectomy
  - Ovarian transposition
  - Ovarian cryopreservation
- Function preservation
  - Sentinel node dissection
  - Nerve sparing radical hysterectomy
  - Mesometrial resection
- Minimal access
  - Laparoscopic
  - Laparoscopically assisted

Radical Trachelectomy

Vaginal

Abdominal

Radical Trachelectomy

- Partial trachelectomy in the elderly patient with abnormal cytology.

Krebs et al. Obstet Gynecol. 1985 Apr;65(4):579-84

- Radical trachelectomy *Daniel Dargent 1987, 1994*

- Abdominal radical trachelectomy *Smith et al. 1996, Rodriguez et al. 2001*

Vaginal radical trachelectomy.

- 72 patients treated by a LPLND followed by VRT
- Stage IA2 (32%) or (60%) IB1
- Mean follow up 60 months
- 2 recurrences (2.8%) and one death (1.4%).
- The actuarial recurrence-free survival is 95%.
- Tumor size >2 cm was statistically significantly associated with a higher risk of recurrence (P = 0.03).

Plante M, Renaud MC, Francois H, Roy M. Gynecol Oncol. 2004 Sep;94(3):614-23.

Vaginal radical trachelectomy.

- A series of 50 pregnancies in 31 women
- The rate of miscarriage 20% was
- 28 (78%) delivered at term (>37 weeks)
- 2 neonatal deaths
- 7 patients (10%) had infertility problems

Plante M, Renaud MC, Hoskins IA, Roy M. Gynecol Oncol. 2005 Jul;98(1):3-10.

Vaginal radical trachelectomy.

Shepherd et al. BJOG June 2006

- 123 women
- Follow up for of 45 months.
- 11 (8.9%) had completion treatment (2 radical hysterectomies and 9 chemoradiotherapy).
- 3 recurrences (2.7%) among the women who did not have completion treatment and 2 (18.2%) in those who did.
- 6 perioperative and 26 postoperative complications.

Vaginal radical trachelectomy.

Shepherd et al. BJOG June 2006

- 63 women attempted pregnancy.
- 55 pregnancies in 26 women
- 28 live births in 19.
- 2 women had continuing pregnancies.
- The 5-year cumulative pregnancy rate among women trying to conceive was 52.8%.
- All but 2 women were delivered by classical caesarean section and 7(25.0%) babies were born at 31+6 weeks or less.

Radical trachelectomy

- Successful pregnancy following radical trachelectomy and in vitro fertilisation with ovum donation.

Kay TA, Renninson JN, Shepherd JH, Taylor MJ. BJOG. 2006 Aug;113(8):965-6.

- Abdominal radical trachelectomy during pregnancy to preserve pregnancy and fertility.

(5 cases and delivery of two healthy babies)

Ungar L, Smith JR, Palfalvi L, Del Priore G. Obstet Gynecol. 2006 Sep;108:811-4.

Radical vaginal trachelectomy (RVT)

- German Multicenter Trial (AGO)
- 108 patients (1A1, = 18, 1A2 n = 21, 1B1 n = 69).
- 8 patients were excluded after RVT (tumor size >2 cm, neuroendocrine tumor type, tumor-involved resection margins, or positive pelvic lymph nodes).
- 100 patients were evaluable
- Median follow-up was 29 (1-128) months.
- 3 (3%) recurrences.
- The projected 5-year recurrence-free and overall survival rates were 97% and 98%.
- The average duration of surgery was 253 (115-402) min.

Hertel et al.,Gynecol Oncol. 2006 Nov;103(2):506-11

Neoadjuvant chemotherapy followed by vaginal radical trachelectomy in bulky stage IB1 cervical cancer: case report

- 3 young women with large cervical lesions.
- They all had lesions measuring 3 to 4 cm and felt to be too big to safely undergo a radical trachelectomy

Plante et al., Gynecol Oncol. 2006 May;101(2):367-70.

Radical trachelectomy

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Ovarian conservation

Ovarian transposition

Ovarian cryopreservarion

Ovarian transposition

- Lateral ovarian transposition. Ovarian relocation in patients with Hodgkin's disease.
  Nahhas et al. Obstet Gynecol. 1971 Nov;38(5):785-8.

- Transposition of the ovaries for function preservation in radical surgery and post-irradiation of cervical carcinoma *Bilek & Leitsmann 1984*

- Heterotopic ovarian auto-transplantation *Muller et al. 1988*

Ovarian transposition

- Can be achieved laparoscopically
- Loss of function 17-50%
- Symptomatic ovarian cysts 24% (3 fold rise)

Chambers et al. 1990

- Ovarian metastasis on transposed ovary
  - This procedure should not be performed in patients with bulky tumor and/or in patients with LVSI.

Morice et al. Gynecol Oncol. 2001 Dec;83(3):605-7

Ovarian transplantation

Tamara the first child born after ovarian transplant 2004

Ovarian transplantation

- Live birth after orthotopic transplantation of cryopreserved ovarian tissue.

Donnez et al. Lancet. 2004 Oct 16-22;364(9443):1405-10.

- Ovarian transplantation between monozygotic twins discordant for premature ovarian failure

Silber et al. NEJM July 2005; 353:58-63 .

- **Pregnancy after transplantation of cryopreserved ovarian tissue in a patient with ovarian failure after chemotherapy.**

Meirow et al. NEJM. 2005 Jul 21;353(3):318-21. 2005

Ovarian cryopreservation

- Live birth after orthotopic transplantation of cryopreserved ovarian tissue.

Donnez et al. Lancet. 2004 Oct 16-22;364(9443):1405-10. van Langendonckt A.

- Ovarian transplantation between monozygotic twins discordant for premature ovarian failure

Sherman et al. NEJM July 2005; 353:58-63 .

Ovarian cryopreservation

- It is unavoidable now to discuss the matter of future fertility in women having cervical cancer in their reproductive years
- Gynaecological oncology centers should make arrangements for these surgical options possible

Function preservation

Nerve sparing radical hysterectomy
Mesometrial resection
Sentinel node dissection

Appropriate management plans would consider:

-Preservation of body image

-Avoidance of crippling therapy complications

-Maintaining feminine integrity & sexual function

-Minimizing institutionalisation & hospital stay

-Reasonable consideration of women's wishes and views

Nerve sparing radical hysterectomy

Pelvic autonomic nervous system:

1.Hypogastric nerves (sympathetic)
Bladder compliance, urinary continence, small muscle contraction during orgasm

2.Pelvic splanchnic nerves (parasympathetic S2-4)
Detrusor contractility, rectal functions, vaginal lubrication & genital swelling during arousal

Nerve sparing radical hysterectomy

Radical hysterectomy results in bladder denervation which is more sympathetic than parasympathetic leading to:

-Detrusor hypertonus

-Uninhihbited detrusor contractions

-Bladder desenstization to filling (63% at 1 year)

-Decreased bladder compliance (two thirds)

-Voiding difficulty (85%)

(Forney et al., 1987, Ralph et al.; 1988)

Nerve sparing radical hysterectomy

The concept of **nerve sparing radical surgery** has been known for decades

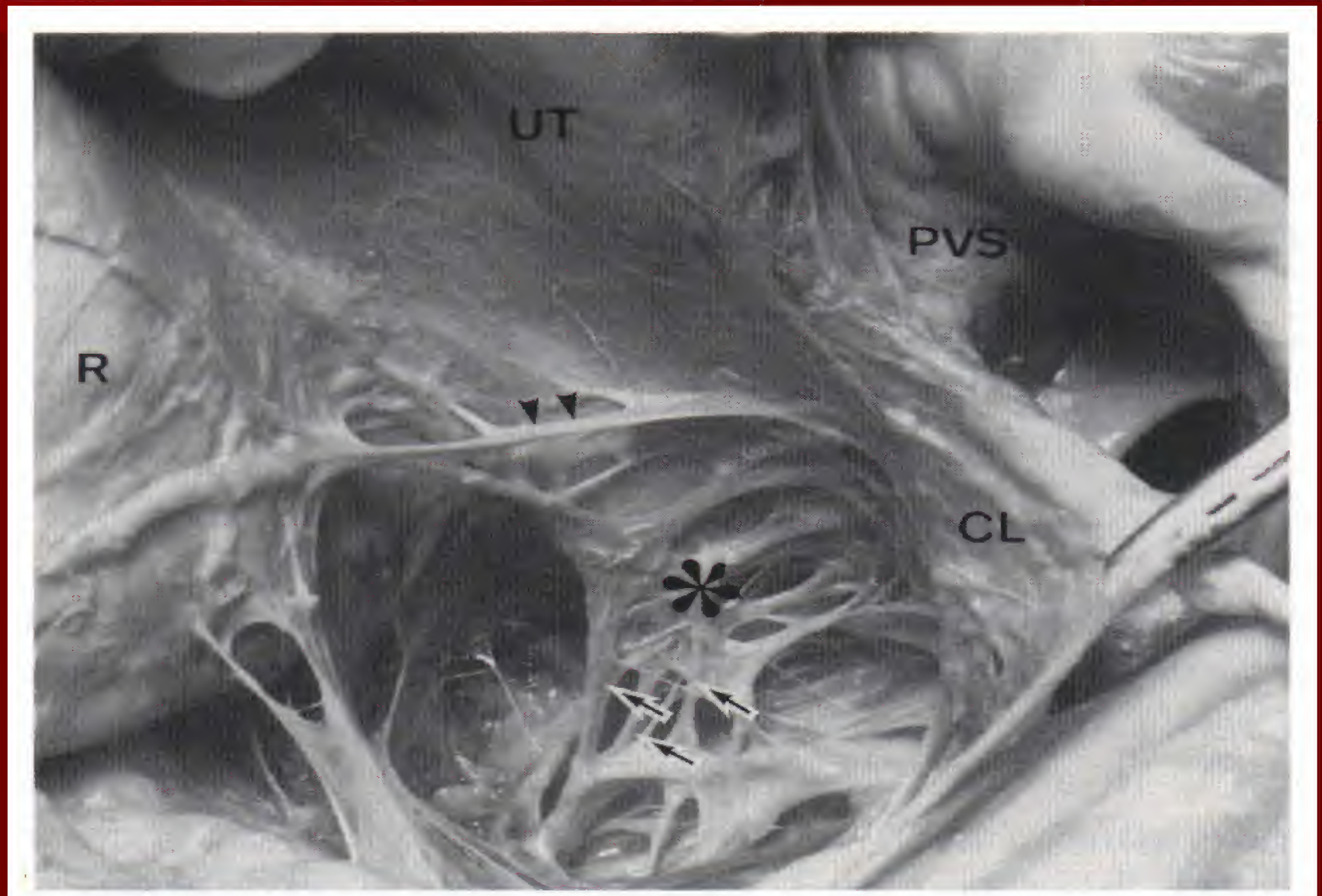
among the Japanese in the treatment of uterine cancer (Tokyo technique)

&

among colorectal surgeons in the treatment of rectal cancer

without compromising outcomes

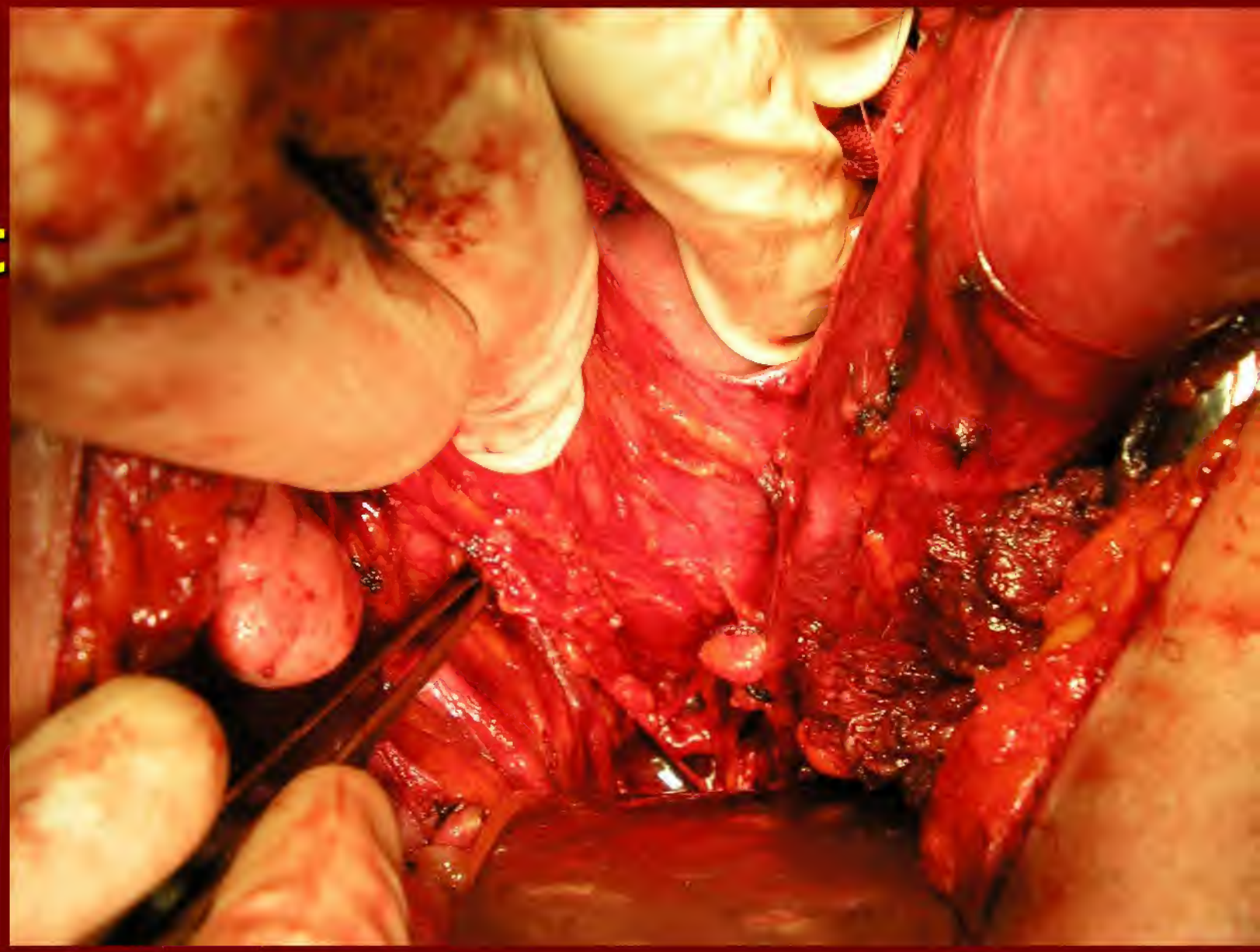
Nerve sparing radical hysterectomy



Nerve sparing radical hysterectomy

Ain Shams Gynecologic Oncology Unit

- 4 patients
- Obesity is an obstacle
- Prolonged bladder recovery in 2



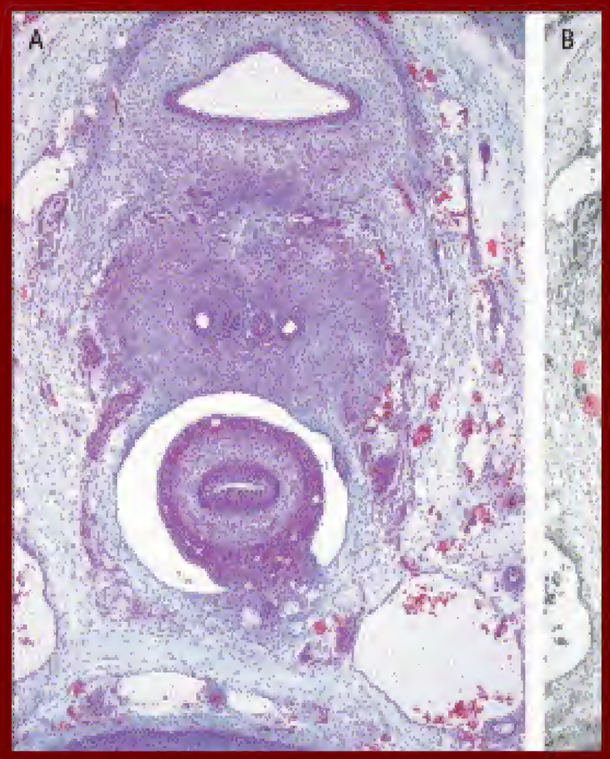
Total Mesometrial Resection

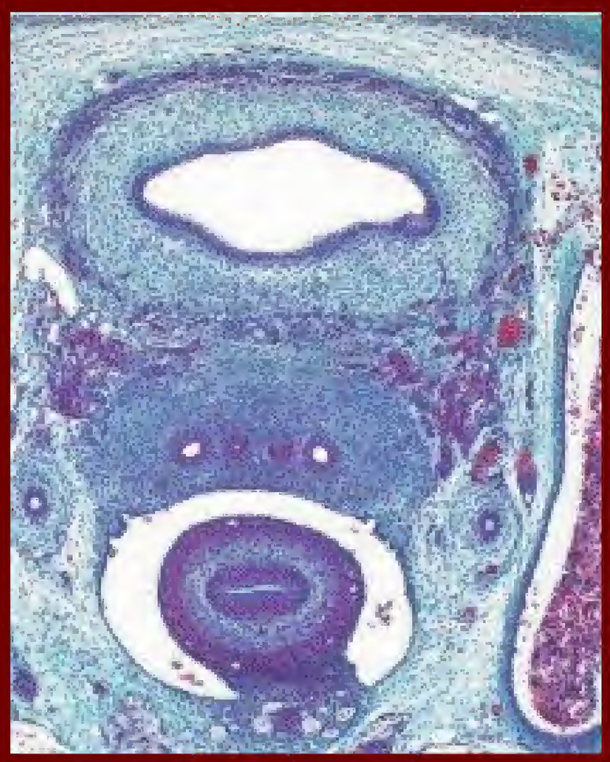
Hockel et al. The Lancet Sept 8 2005

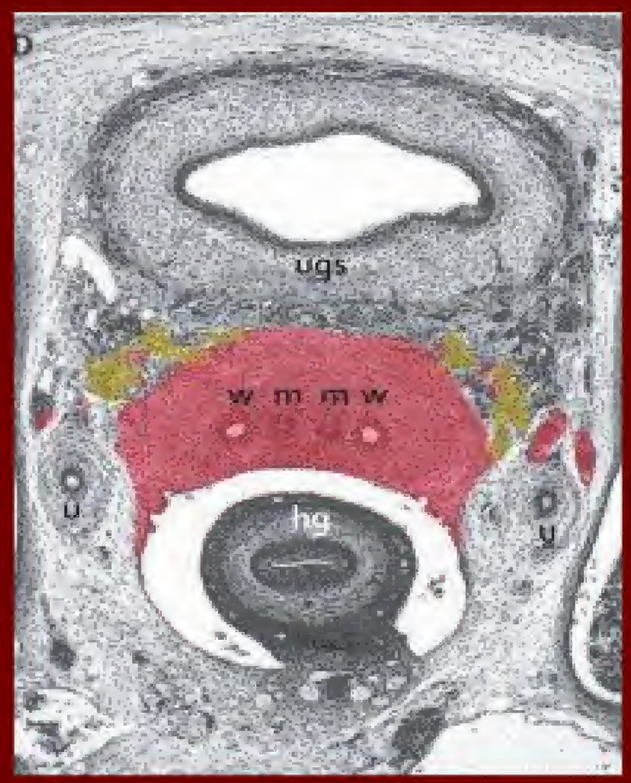
Macroscopic, microscopic, and occult local tumour spread might be restricted to a permissive territory related to the morphogenesis of the tissue or organ from which the tumour originates.

Total mesometrial resection

Hockel et al.The Lancet Sept 8 2005

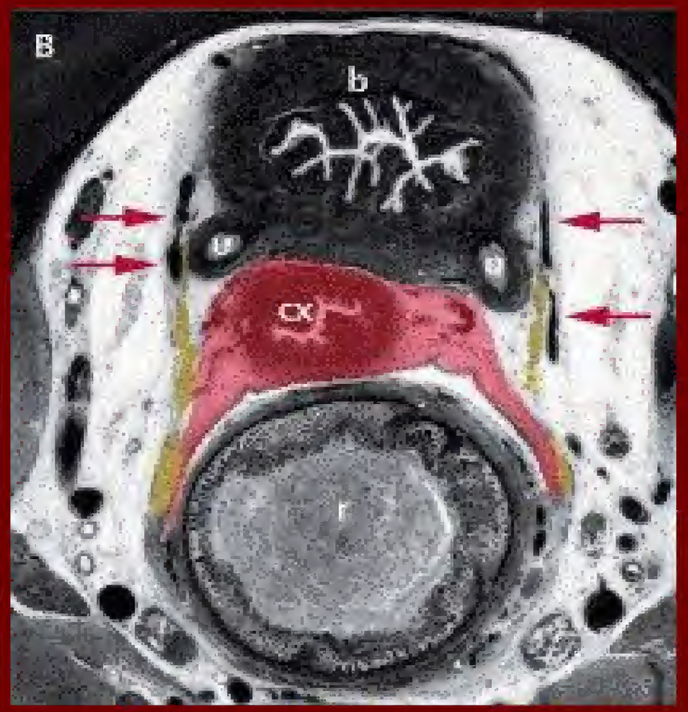


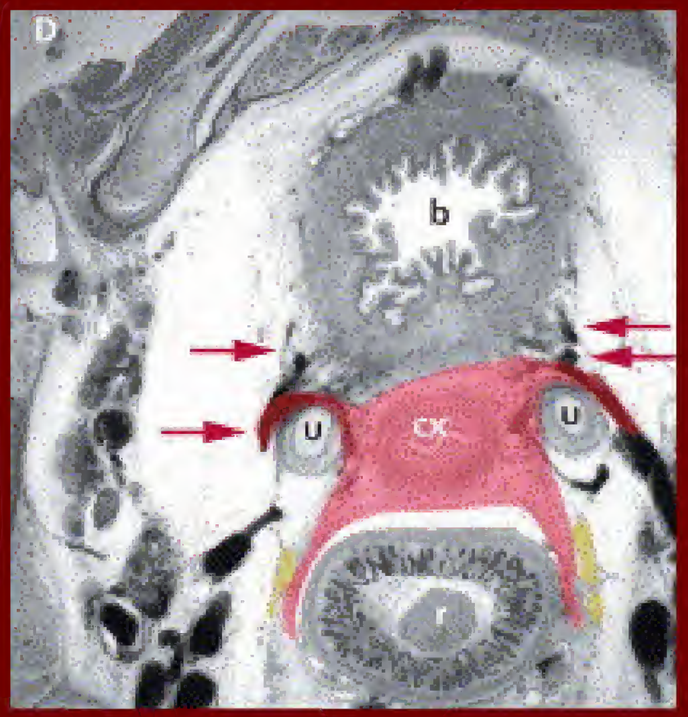




Total mesometrial resection

Hockel et al. The Lancet Sept 8 2005





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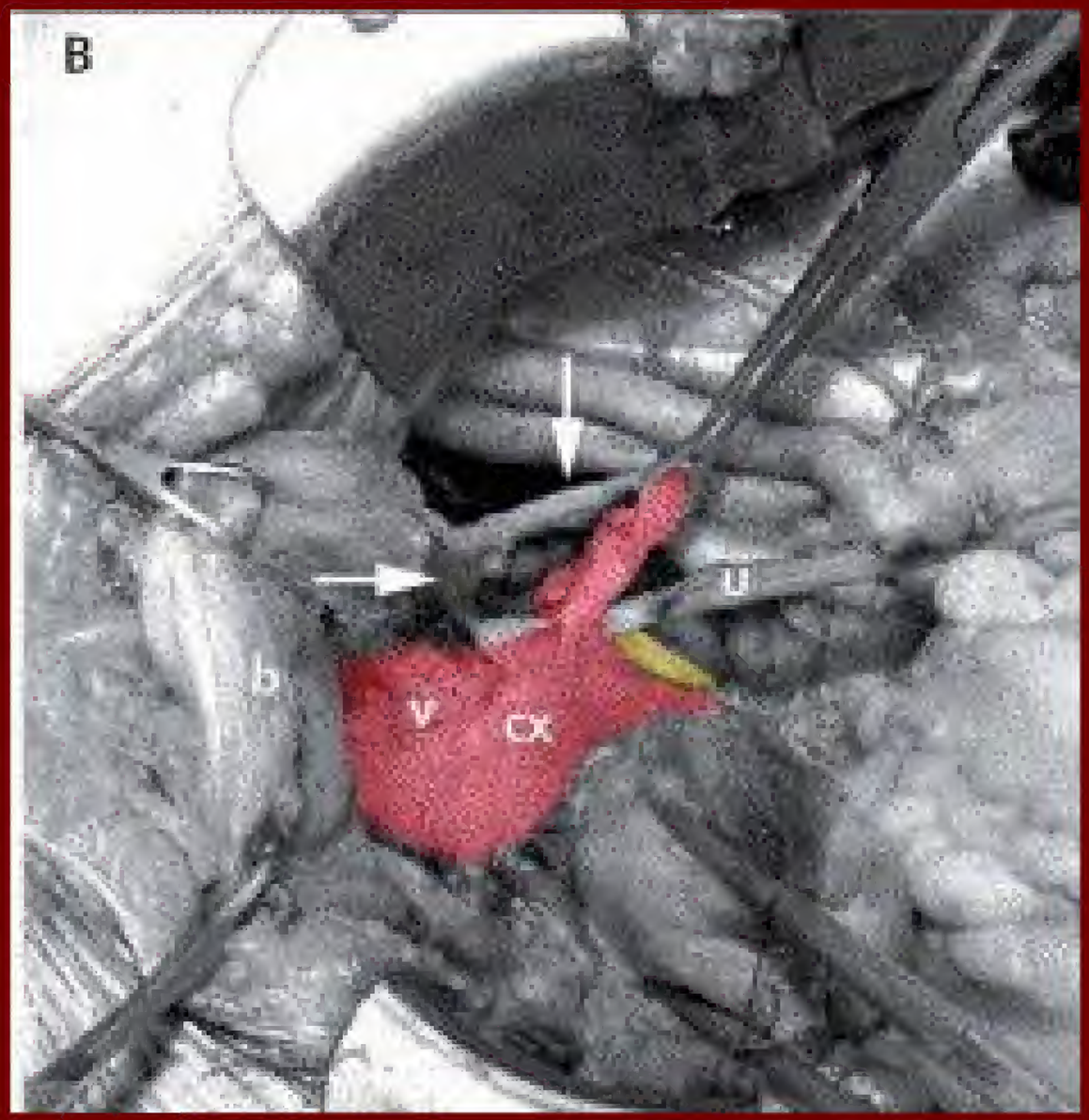

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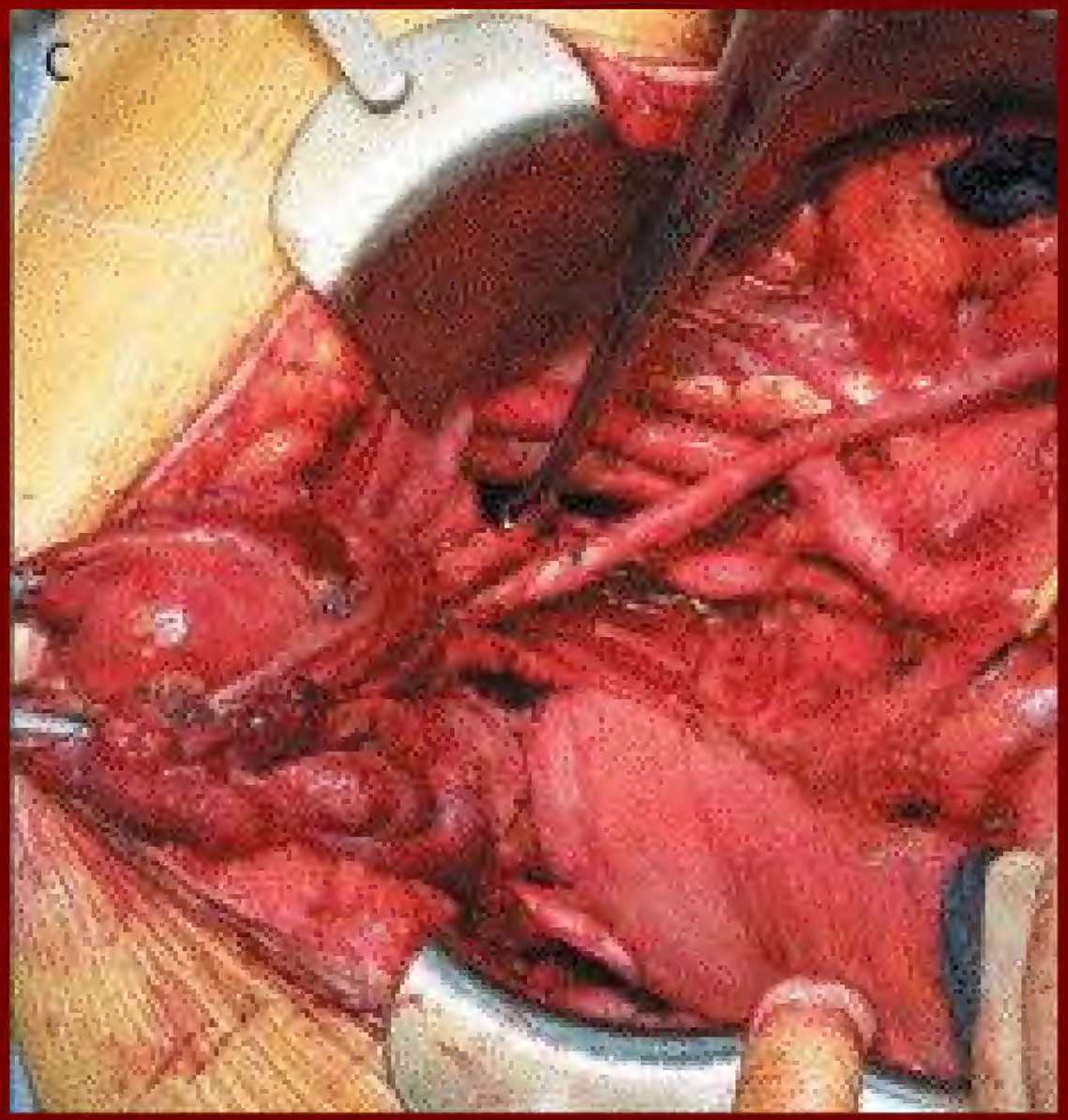

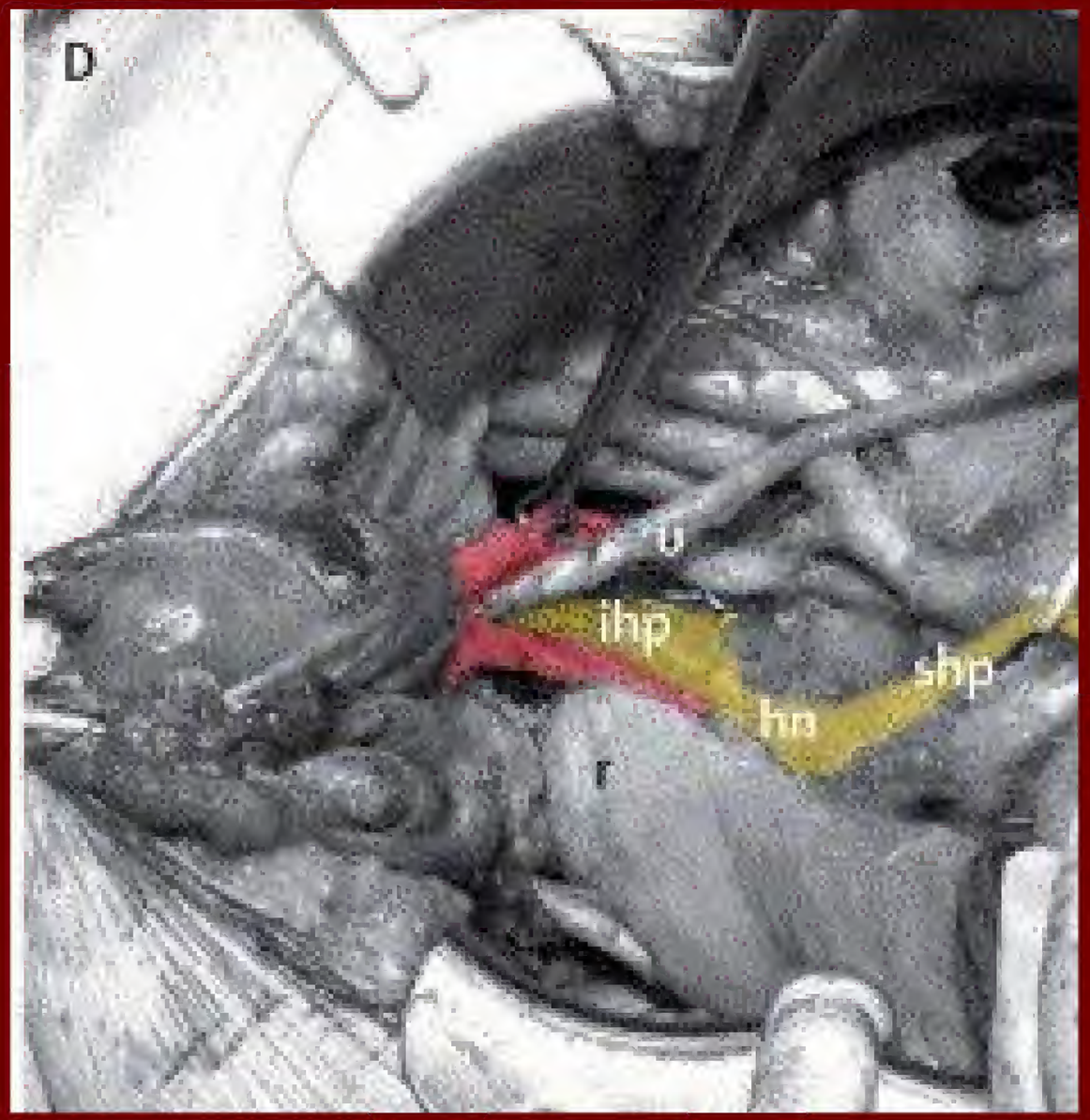

Total Mesometrial Resection

Hockel et al. The Lancet Sept 8 2005

- **Identified morphogenetic unit through which cancer cells spread.**
- **105 of 106 had total mesometrial resection had microscopically tumour-free resection margins**
- **48 (96%) of 50 patients had pelvic recurrence-free survival at 3 years (95% CI 92–100)**

Sentinel node dissection
in cervical cancer

- Blue dye or Technetium-99m-labeled colloid

- Feasible
  - Dargent et al. 2000 (35 patients)
  - van Dam et al. 2003 (25 patients)
  - Di Stefano et al. 2005 (45 patients)
  - Rob et al. 2007 (26 patients)

Sentinel node dissection
in cervical cancer

- Conflicting efficiency

  Cytokeratin immuno-histochemistry may identify lymph node micro-metastases in non-sentinel lymph nodes even when sentinel lymph nodes were found to be negative for disease on biopsy (NPV 87.5%)

Marchiole et al. Cancer. 2004 May 15;100(10):2154-9.

Laparoscopic sentinel lymph nodes identification followed by trachelectomy

- Laparoscopic sentinel lymph nodes identification followed by trachelectomy in early stage cervical cancer (one case)

Barwijuk AJ, Gawlak M. Ginekol Pol. 2006 Jul;77(7):550-4.

Less radical fertility-sparing surgery than radical trachelectomy in early cervical cancer

- 26 patients (6-IA2, 20-IB1)
- laparoscopic lymphadenectomy with sentinel lymph node identification (SLNI) followed by large cone or simple trachelectomy after 7 days in node negative
- No false negative SLNI
- 15 women planned pregnancy
- 11 women became pregnant (15 pregnancies)
- 7 women delivered eight children (3 (43%) preterm)

Rob L, Charvat M, Robova H, Pluta M, Strnad P, Hrehorcak M, Skapa P. Int J Gynecol Cancer. 2007 Jan-Feb;17(1):304-10

Minimal access

Laparoscopic procedures
Laparoscopically assisted procedures

Laparoscopic procedures

- Laparoscopic-assisted vaginal radical hysterectomy (LARVH) *Dargent et al. 1995 Roy et al. 2005*
- Total laparoscopic radical parametrectomy (TLRP) *Lee and Huang 2005*
- Total laparoscopic radical hysterectomy *Gil-Moreno et al. 2005*
- Laparoscopic trachelectomy
- Laparoscopic pretreatment surgical staging *Chang et al. 2005*

Laparoscopic procedures

- High level skill requirements
- Port metastases
- The feasibility is established from cohort or case-control.
- The absence of large phase III studies

Conclusion

- Surgical management of cervical carcinoma is witnessing a diverse evolution of a more refined and precise radicality with valid and viable options to preserve reproductive capacities.

- This entails better patient counseling and more collaborative multi disciplinary approaches in planning management.

Conclusion

- Of course there is a great demand for training to acquire skills necessary to efficiently perform of these evolving surgical techniques.
- Effectiveness of new techniques needs to be appropriately evaluated through RCT

Thank You